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| EXAMINER | |
|---|---|
| HUGHES, ALICIA R | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1614 | |

| NOTIFICATION DATE | DELIVERY MODE |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

INFO@ORTPATENT.COM

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/798,119 | CHUNG, YIH-LIN | |
| | Examiner | Art Unit | |
| | ALICIA R. HUGHES | 1614 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *25 June 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-4 and 6-21* is/are pending in the application.

4a) Of the above claim(s) *3,6-10,12,13 and 18-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-2, 4, 11 and 14-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1 sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Status of the Claims and Examination*

Claims 1-4 and 6-21 are pending currently. However, only claims 1, 11, and 14-17 are the subject of this Office Action, as claims 2-4, 6-10, 12, 13, and 18-21 are withdrawn from consideration, being drawn to a non-elected invention. See 37 C.F.R. 1.142(b).

Applicant's arguments and amendments filed on 25 June 2009 have been fully considered. Rejections and objections not reiterated from previous office actions are hereby withdrawn.

Upon reconsideration of the pending claims, as presented, the following new rejections are applied. They constitute the complete set of rejections being applied to the instant application presently.

### *Claim Rejections – 35 U.S.C. §112.1*

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

***First New Matter Rejection***

Claims 1, 11, and 14-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the

relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

A review of application as filed does not disclose the invention embodied by the present set of claims as a result of the removal of this limitation.

In reviewing the written basis for claim 1, particularly sub-part (i) in the specification as originally filed, on page 3, lines 6-13, requires "simultaneously (1) enhancing the suppression of tumor or proliferating cell growth in a host on need of radiotherapy and/or chemotherapy, *and* (2) preventing the onset of or ameliorating the radiation- and/or chemotherapy-induced complications or sequalae of mucositis, dermatitis, ulceration, fibrosis, xerostomia, plantar-palmar syndrome, and tumorigenesis" (emphasis added). However, instant claim 1 at present only indicates that the therapeutic gain is the item (2) of said page 3 specification citation and does not require said item (1), thus altering the requirement for simultaneity and in a manner not contemplated as filed.

In light of the foregoing, claims 1, 11, and 14-17 are rejected, because they contain new matter not supported by the specification. This is a new matter rejection.

***Second New Matter Rejection***

Claims 1, 11, and 14-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the

relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Further review for the written basis as in claim 2, as originally filed at least requires a high probability of tumor control "with" a low frequency of sequelae. Further, the only protecting normal tissue(s) from cell death as originally filed is in the original claim 2, penultimate line, which depends from original claim 1, also requires item (1) but is not required in instant claim 1 regarding any items (i), (ii), or (iii). Thus instant claim 1, contains a broadening of the subject matter in a manner not previously contemplated.

In light of the foregoing, claims 1, 11, and 14-17 are rejected, because they contain new matter not supported by the specification. This is a new matter rejection.

***Third New Matter Rejection***

Claims 1, 11, and 14-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In reviewing the claims, the only written basis for the instant claim 1, part (iii) in the specification as originally filed, is on page 3 at lines 14-22. Said part (iii) is only associated with histone "deacetylase inhibitor" effects and not with the generic histone "hyperacetylating agent"

treatment. Thus, part (iii) being generically associated with the broad administration of a histone hyperacetylating agent constitutes new matter as it was not aptly considered in the specification.

In light of the foregoing, claims 1, 11, and 14-17 are rejected, because they contain new matter not supported by the specification. This is a new matter rejection.

***Claim Rejections – 35 U.S.C. §103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 11, and 14-16 are rejected under 35 U.S.C. 103(a) as being obvious over U.S. Patent No. 5,877,213 [hereinafter referred to as "Samid"].[1]

This Office's arguments from its actions of 23 March 2007, 01 October 2007, 08 April 2008 and 15 April 2009 are incorporated herein by reference in their entirety.

Applicant continues to argue that the claims are directed to the treatment of side effects to be treated as a direct consequence of chemotherapy or radiotherapy and not from the underlying cancer state itself "as mistakenly believed by the Examiner" (Applicant's arguments of 31 July 2009 at page 7 of 10, para 1). Applicant further argues that sodium phenylacetate, and its derivatives including sodium phenylbutyrate, administration in cancer patients results in concentration-dependent cell growth arrest and can cause an inhibition of growth to primary

human skin FS4 fibroblasts and as a result, administration of the same would "aggravate skin tissue damage by inhibiting skin cell growth." *Id.* Applicant goes on further to argue that even if a prima facie case of obviousness has been established, unexpected results produced would render the invention non-obvious nevertheless. *Id.* at page 8 of 10.

The above arguments are not deemed persuasive for the reasons of record set forth in this Office's previous actions mentioned *supra*. Further, with regard to Applicant's reference to "concentration-dependent cell growth arrest" and "human skin FS-4 fibroblasts, it is important to note that these are subsets of cells rather than all cells and therapeutic gain in tissue necrosis necessarily may be possible through the arrest of non-desirous cells. Further, the leap to the conclusion by Applicant that "a skilled person in the art would have readily known that NaPA and derivatives thereof (e.g., NaPB) would aggravate skin tissue damage by inhibiting skin cell growth" (See Page 7 of 10, last paragraph) is a leap that appears as no more than a mere allegation that lacks sound factual support.

Finally, as noted previously, claims are to be given their broadest reasonable interpretation and regardless of Applicant's assertion that the claims are directed to the treatment of side effects, the the claims as written in this application, apply for increasing therapeutic gain associated with a host of conditions, including tissue necrosis, for example, where a patient undergoes radiotherapy or chemotherapy. Tissue necrosis continues to be a process known to have a correlation has a direct correlation to malignancy and/or nonmalignant dense structures.

By Applicants' own admission, "the claimed method targets subjects (e.g., cancer patients) who suffer from certain side effects" (Page 9 of Applicants' Remarks). Thus, the

[1] Cited on PTO Form 892 filed on 23 March 2007.

patient population in Samid et al and in the instant case may be construed as one in the same. Further, the claims are directed to a "subject in need" and this particular population of need is the population of cancer patients.

With regard to Applicant's claim of unexpected results, while the argument is appreciated, the same is not persuasive, because the inhibition of cells are those of a malignant nature that as noted prior by the Applicant is "concentration dependent" rather than all cells. Further, the arrest of some cells does not preclude the growth of other cells, which again would lead to therapeutic gain.

In light of the foregoing, it would have been *prima facie* obvious to one of ordinary skill in the art to administer sodium phenylbutyrate in the manner prescribed by Samid, in combination with radiotherapy, as a method of treating tissue necrosis.

***Conclusion***

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alicia Hughes whose telephone number is 571-272-6026. The examiner can normally be reached from 9:00 AM to 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached at 571-272-0718. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR of Public PAIR. Status information for unpublished applications is available through Public PAIR only. For information about the PAIR system, see http://pair-direct-uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Alicia R. Hughes/
Examiner, Art Unit 1614

/James D Anderson/
Primary Examiner, Art Unit 1614